

REMARKS

In the spirit of cooperation, to advance Applicants' remaining rejected claims into an allowance with claims 18-23 for which allowability has already been indicated, Applicants and the undersigned have amended independent claim 9 by removing the correlation with carcinoma. As such, the assay of claim 9 is enabled.

By amending independent claim 9 hereby, Applicants and the undersigned will have further distinguished all remaining claims 10-17 that also depend from and further narrow the scope of amended, independent claim 9.


Applicants have amended claims 15 and 16 to correct a typographical error. An error in the dependency of claim 12 was also detected and corrected hereby such that it now accurately depends from claim 9 instead of claim 11. In addition, Applicants have added claims 24-31 which are identical to claims 10-17 and depend from allowed, independent claim 18. Claim 18 was originally dependent on claim 9 and included claims 10-17. Claims 24-31 further narrow the scope of allowed, independent claim 18 and do not raise any new matter.

Accordingly, it is respectfully requested that with the foregoing timely amendments to claims 9-17, the enablement rejection of same should be reconsidered and withdrawn causing claims 9-17 to join previously allowable claims 18-23. Applicants also respectfully request that new claims 24-31 join the previously allowable claims 18-23. A three month extension of time and the appropriate fees are also submitted herewith.

Respectfully submitted,

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By



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Version with Markings to Show Changes Made:

Claim 1 (withdrawn): An isolated nucleic acid selected from the group consisting of:

- a) a nucleic acid which encodes a protein comprising the amino acid sequence SEQ ID NO. 1,
- b) a nucleic acid which encodes a protein comprising an amino acid sequence which is at least 90% identical to SEQ ID NO. 1 and which has at least 50% of the biological activity of the protein SEQ ID NO. 1,
- c) a nucleic acid which is complementary to nucleic acid a) or b).

Claim 2 (withdrawn): The isolated nucleic acid of claim 1 wherein the nucleic acid has the sequence SEQ ID NO. 2.

Claim 3 (withdrawn): The isolated nucleic acid of claim 1 wherein the nucleic acid encodes a protein comprising the amino acid sequence SEQ ID NO. 3.

Claim 4 (withdrawn): The isolated nucleic acid of claim 1 wherein the nucleic acid encodes a protein comprising an amino acid sequence which is at least 99% identical to SEQ ID NO. 1.

Claim 5 (withdrawn): The isolated nucleic acid of claim 4 wherein the encoded protein comprises an amino acid sequence selected from the group consisting of SEQ ID NO. 4, SEQ ID NO. 5, and SEQ ID NO. 6.

Claim 6 (withdrawn): An immunogenic conjugate comprising an immunogenic carrier molecule and a polypeptide of between 10 and 500 amino acids in length comprising an amino acid sequence of 10 to 25 amino acids in length which is identical to an amino acid sequence of the same length contained in an amino acid sequence selected from the group consisting of amino acids 628-705 of SEQ ID NO. 1, amino

acids 628-705 of SEQ ID NO. 4, amino acids 628-705 of SEQ ID NO. 5, and amino acids 628-705 of SEQ ID NO. 6.

Claim 7 (withdrawn): The immunogenic conjugate of claim 6, wherein the polypeptide comprises an amino acid sequence of 11 to 21 amino acids in length which is identical to an amino acid sequence of the same length contained in an amino acid sequence selected from the group consisting of amino acids 628-705 of SEQ ID NO. 1, amino acids 628-705 of SEQ ID NO. 4, amino acids 628-705 of SEQ ID NO. 5, and amino acids 628-705 of SEQ ID NO. 6.

Claim 8 (withdrawn): The immunogenic conjugate of claim 6, wherein the immunogenic carrier molecule is selected from the group consisting of keyhole limpet hemocyanin and bovine serum albumin.

Claim 9. (As further amended herein) An assay for determining the concentration of epidermal growth factor receptor in a biological sample from a human patient, the assay comprising:

- a) obtaining a biological sample from the patient;
- b) contacting an amount of a first purified antibody that specifically reacts with a first epitope of the extracellular ligand binding domain of sErbB1 with the patient biological sample to be tested, wherein the first purified antibody is modified with a first labeling moiety;
- c) contacting the sample with an amount of a second purified antibody that specifically reacts with a second epitope of the extracellular ligand binding domain of sErbB1, wherein the second purified antibody is modified with a second labeling moiety, and wherein the second purified antibody does not competitively inhibit the binding of the first purified antibody; [and]
- d) detecting the co-presence of the first and second labels to determine the concentration of the epidermal growth factor receptor complexed with the antibodies; wherein one of the antibodies is chosen from the group consisting of: MAb R.1 and antibodies with competitively inhibit the binding of MAb R.1 to ErbB1; and wherein the

other antibody is chosen from the group consisting of MAb 528 and antibodies which competitively inhibit the binding of MAb 528 to ErbB1; and

e) comparing the concentration of epidermal growth factor receptor obtained in step d) with a normal value[; and]_

~~f) correlating a decrease in the concentration of epidermal growth factor receptor in the patient biological sample with the presence of a carcinoma in the patient.~~

Claim 10 (original): The assay of claim 9 wherein the patient biological sample is chosen from the group consisting of urine and ascites.

Claim 11 (Previously amended): The assay of claim 9 wherein the patient biological sample is chosen from the group consisting of blood, serum and plasma.

Claim 12: (currently amended): The assay of claim [11] 9 wherein the first labeling moiety is an affinity binding moiety.

Claim 13 (original): The assay of claim 12 wherein the affinity binding moiety is biotin.

Claim 14 (original): The assay of claim 13 wherein detection of the presence of the first labeling moiety is by binding of the biotin moiety to a solid support coated with a molecule chosen from the group consisting of streptavidin and avidin.

Claim 15 (currently amended): The assay of claim 9 wherein the second ~~labelling~~ labeling moiety is selected from the group consisting of a fluorescent moiety, a colorigenic moiety, and a chemiluminescent moiety.

Claim 16 (currently amended): The assay of claim 9 wherein the second ~~labelling~~ labeling moiety is acridinium.

Claim 17 (original): The assay of claim 16 wherein the detection of the presence of the second labeling moiety is by measuring light emitted from a chemiluminescent reaction utilizing the second labeling moiety.

Claim 18 (previously amended): An assay for determining the concentration of epidermal growth factor receptor in a biological sample from a female patient, the assay comprising:

- a) obtaining a biological sample from the female;
- b) contacting an amount of a first purified antibody that specifically reacts with a first epitope of the extracellular ligand binding domain of sErbB1 with the biological sample to be tested, wherein the first purified antibody is modified with a first labeling moiety;
- c) contacting the sample with an amount of a second purified antibody that specifically reacts with a second epitope of the extracellular ligand binding domain of sErbB1, wherein the second purified antibody is modified with a second labeling moiety, and wherein the second purified antibody does not competitively inhibit the binding of the first purified antibody;
- d) detecting the co-presence of the first and second labels to determine the concentration of the epidermal growth factor receptor complexed with the antibodies; wherein one of the antibodies is chosen from the group consisting of: Mab R.1 and antibodies which competitively inhibit the binding of Mab R.1 to ErbB1; and wherein the other antibody is chosen from the group consisting of Mab 528 and antibodies which competitively inhibit the binding of Mab 528 to ErbB1.
- e) comparing the concentration of soluble epidermal growth factor receptor obtained in step d) with a normal value; and

f) correlating a decrease in the concentration of soluble epidermal growth factor receptor in the patient biological sample with the presence of an ovarian carcinoma in the patient.

Claim 19 (original): The assay of claim 18 wherein the normal value is obtained by assaying biological samples from females of approximately the same age as the patient.

Claim 20 (original): The assay of claim 18 further comprising the step of performing a second assay on a biological sample obtained from the patient at a point in time after the initial assay.

Claim 21 (original): The assay of claim 20, wherein the patient has undergone treatment for ovarian cancer selected from the group consisting of chemotherapy, radiation therapy, and surgical treatment in the interval between the initial and second assay.

Claim 22 (original): The assay of claim 20, further comprising the step of correlating an increase in the concentration of soluble epidermal growth factor receptor in the patient biological sample with an improved prognosis in the ovarian cancer condition.

Claim 23 (original): The assay of claim 20, further comprising the step of correlating a decrease in the concentration of soluble epidermal growth factor receptor in the patient biological sample with an declining prognosis in the ovarian cancer condition.

Claim 24 (new): The assay of claim 18 wherein the patient biological sample is chosen from the group consisting of urine and ascites.

Claim 25 (new): The assay of claim 18 wherein the patient biological sample is chosen from the group consisting of blood, serum and plasma.

Claim 26: (new): The assay of claim 18 wherein the first labeling moiety is an affinity binding moiety.

Claim 27 (new): The assay of claim 26 wherein the affinity binding moiety is biotin.

Claim 28 (new): The assay of claim 27 wherein detection of the presence of the first labeling moiety is by binding of the biotin moiety to a solid support coated with a molecule chosen from the group consisting of streptavidin and avidin.

Claim 29 (new): The assay of claim 18 wherein the second labeling moiety is selected from the group consisting of a fluorescent moiety, a colorigenic moiety, and a chemiluminescent moiety.

Claim 30 (new): The assay of claim 18 wherein the second labeling moiety is acridinium.

Claim 31 (new): The assay of claim 30 wherein the detection of the presence of the second labeling moiety is by measuring light emitted from a chemiluminescent reaction utilizing the second labeling moiety.